

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method of producing insulinotropic GLP-1 (7-36) polypeptide and/or GLP-1 analogs comprising:

(a) introducing into a DNA fragment a first and second individual restriction endonuclease cleavage sites capable of forming a hybrid site to two terminals of a gene which encodes either the GLP-1(7-36) polypeptide or GLP-1 analogs, respectively, and a third restriction endonuclease cleavage site located outside of the region between said first and second restriction endonuclease cleavage sites, wherein ~~so that~~ the second restriction endonuclease cleavage site is located between the first and third restriction endonuclease cleavage sites;

(b) digesting the ~~gene~~ DNA fragment of step (a) with restriction endonucleases at the first and third restriction endonuclease cleavage sites and ligating said digested ~~gene~~ DNA fragment ~~into~~ with a vector, wherein said vector has the second and third restriction endonuclease cleavage sites and is digested at said second and third restriction endonuclease cleavage sites before said ligation;

(c) repeating step (b) to form an expression vector comprising N copies of ~~a resulting series-linked~~ GLP-1(7-36) gene, GLP-1 analog gene, or a combination of GLP-1(7-36) gene and GLP-1 analog genes, wherein N is an integer from 2 to 32;

(d) transforming said expression vector ~~containing the series-linked gene~~ into a host cell;

(e) expressing in the host cell a protein comprising N copies of the ~~series-linked~~ GLP-1(7-36) polypeptide, GLP-1 analog, or the combination thereof, but without any carrier protein;

(f) breaking up the host cell and cleaving said protein of step (e) to obtain GLP-1 (7-36) polypeptides or GLP-1 analogs that are capable of stimulating the secretion of insulin; and

(g) separating and purifying said GLP-1 (7-36) polypeptides or GLP-1 analogs.

2. (Previously presented) The method according to claim 1 wherein the two restriction endonucleases capable of forming a hybrid site are Bgl II and BamH I.

3. (Previously presented) The method according to claim 1 wherein the two restriction endonucleases capable of forming a hybrid site are Sal I and Xho I.

4. (Currently amended) The method according to claim 1 in which said vector contains N copies of the GLP-1 (7-36) gene, GLP-1 analog gene, or a combination of GLP-1 (7-36) gene and GLP-1 analog gene ~~series-linked gene~~, wherein N is ~~4~~ an integer from 4 to 32.

5. (Currently amended) The method according to claim ~~1~~ 4 in which the said vector contains N copies of the GLP-1 (7-36) gene, GLP-1 analog gene, or a combination of GLP-1 (7-36) gene and GLP-1 analog gene ~~series-linked gene~~, wherein N is an integer from 8 to 32.

6. (Currently amended) The method according to claim 5 in which the said vector contains N copies of the GLP-1 (7-36) gene, GLP-1 analog gene, or a combination of GLP-1 (7-36) gene and GLP-1 analog gene ~~series-linked gene~~, wherein N is 16.

7. (Currently amended) The method according to claim 5 in which the said vector contains N copies of the GLP-1 (7-36) gene, GLP-1 analog gene, or a combination of GLP-1 (7-36) gene and GLP-1 analog gene~~-series-linked-gene~~, wherein N is 32.

8. (Cancelled).

9. (Currently amended) The method according to claim 1 in which said host cell expresses a protein containing N copies of the GLP-1 (7-36) polypeptide, GLP-1 analog, or the combination thereof~~-series-linked polypeptide~~, wherein N is 4~~an integer from 2 to 32~~.

10. (Currently amended) The method according to claim 1~~9~~ in which said host cell expresses a protein containing N copies of the GLP-1 (7-36) polypeptide, GLP-1 analog, or the combination thereof~~-series-linked polypeptide~~, wherein N is an integer from 8 to 32.

11. (Currently amended) The method according to claim 10 in which said host cell expresses a protein containing N copies of the GLP-1 (7-36) polypeptide, GLP-1 analog, or the combination thereof~~-series-linked polypeptide~~, wherein N is 16.

12. (Currently amended) The method according to claim 10 in which said host cell expresses a protein containing N copies of the GLP-1 (7-36) polypeptide, GLP-1 analog, or the combination thereof~~-series-linked polypeptide~~, wherein N is 32.

13. (Previously presented) The method according to claim 9 wherein said host cell is a prokaryotic cell.

14. (Previously presented) The method according to claim 13 wherein said host cell is *Escherichia coli* JM103, JM109, HB101, or DH5α or C600.

15. (Cancelled).

16. (Previously presented) The method according to claim 1 wherein said protein is cleaved at step (f) by clostripain or trypsin.

17-36. (Cancelled)

37. (Currently amended) A method of producing insulintropic GLP-1 (7-36) polypeptide and/or GLP-1 analogs comprising:

(a) introducing into a DNA fragment a first and second individual restriction endonuclease cleavage sites capable of forming a hybrid site to two terminals of a gene which encodes either the GLP-1 (7-36) polypeptide or GLP-1 analogs, respectively, and an third restriction endonuclease cleavage site located outside of the region between said first and second endonuclease cleavage sites, wherein ~~so that~~ the second restriction endonuclease cleavage site is located between the first and third restriction endonuclease cleavage sites;

(b) ~~digesting the gene~~ DNA fragment from step (a) with restriction endonucleases at the first and third restriction endonuclease cleavage sites and ligating said digested ~~gene~~ DNA fragment ~~into~~ with a vector, wherein said vector has the second and third restriction endonuclease cleavage sites and is digested at said second and third restriction endonuclease cleavage sites before said ligation;

(c) repeating step (b) to form an expression vector comprising N copies of ~~a resulting series-linked~~ GLP-1(7-36) gene, GLP-1 analog gene, or a combination of GLP-1(7-36) gene and GLP-1 analog genes, wherein N is an integer from 2 to 32;

(~~ed~~) transforming said expression vector ~~containing the series-linked gene~~
into a host cell; and

(~~de~~) expressing in the host cell a protein comprising N copies of the ~~series-~~
~~linked~~ GLP-1(7-36) polypeptide, GLP-1 analog₁ or the combination thereof, but
without any carrier protein.

38. (Cancelled)

39. (Currently amended) The method according to claim ~~38~~ 37
further comprising the following steps after step (e):

(f) breaking up the host cell and cleaving said protein from step (e) to
obtain GLP-1(7-36) polypeptides or GLP-1 analogs that are capable of stimulating
the secretion of insulin; and

~~(g) separating and purifying said GLP-1(7-36) polypeptides or GLP-1~~
analog_s.